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Studying the Influence of Axial Length on Retinal Nerve Fiber Layer Thickness and Optic Disc Size Measurements by Spectral-Domain OCT

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Abstract: Purpose: The aim of this study is to evaluate the effect of axial myopia on the retinal nerve fiber layer thickness and optic disc size using spectral domain Optical Coherence Topography. **Patients and Methods:** This study was a cross-sectional study on 30 myopic eyes of patients aged between 30-40 years who were coming to the outpatient clinic. The patients were recruited from the outpatient clinic of the Health Insurance Hospital in Suez. **Results:** This study found that the average, superior and inferior retinal nerve fiber layer thickness (RNFLT) significantly decreased with increase of the axial length. This study also found a direct correlation between axial length (AL) and disc area. However, AL was not significantly correlated with RNFL thickness in the nasal or temporal quadrant, optic rim area, or cup disc ratio (CDR). **Conclusion:** The study revealed that AL had a correlation with RNFLT and that axially myopic eyes showed thinner RNFLT than emmetropic eyes.
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Key words: Axial length, retinal nerve fiber layer thickness, optic disc size spectral-domain OCT

1. Introduction

Myopia may result from an eye being either too long or its optical components too powerful, leading to images of distant objects being formed in front of the retina.[1]

Notably, myopia has been widely reported to affect the size and shape of the optic disc and peripapillary retinal nerve fiber layer (RNFL). Diagnosis of glaucoma in myopic patients is thus very challenging.[2]

Thorough and accurate understanding of the relationship between myopia and the anatomic structures of the optic nerve head (ONH) and RNFL is important, particularly in light of the two to three times greater risk of glaucoma in myopic individuals compared with nonmyopic individuals[3].

The retinal nerve fiber is the axon of a retinal ganglion cell (RGC) that carry the visual information and transfer the signals from cone and rod photoreceptors via an RGC to the brain through the ONH[4].

The thickness of the RNFL ranges from about 10 µm (around the fovea) to 400 µm (margin of the ONH) for a healthy human eye. In case of glaucoma, the RNFL thickness is reduced[5].

Optical coherence tomography (OCT) is a noninvasive technology that has been extensively used to evaluate many diseases of the optic nerve. In most cases, scientists have focused their attention on the peripapillary RNFL thickness[6].

However, OCT can also analyze and measure topographic parameters of the ONH, including the disc area, neuroretinal rim area and cup-to-disc ratio[7].

2. Patients and Methods

This is a cross sectional study included 30 myopic eyes in patients with ages from 30-40 years old. The patients were recruited from the outpatient clinic of the Health Insurance Hospital in Suez.

Exclusion criteria

Any retinal abnormalities other than myopia such as retinal vascular diseases & retinal dystrophies. Any other eye diseases such as amblyopia, glaucoma and uveitis. Patients who have a history of intraocular surgery, refractive surgery, or intra-vitreal injection.

Methodology

All patients signed an informed written consent before investigations including type and technique of the procedure. Detailed history was taken from each patient. Each subject underwent a comprehensive ophthalmological evaluation, including visual acuity measurement, best corrected visual acuity (BCVA), slit-lamp examination, intraocular-pressure measurement with Goldmann applanation tonometry, and dilated fundus examination. Axial length was measured using the Zeiss IOL Master 500 (IOL master group; Oberkochen, Germany).

Procedures

After pupil dilation, the eyes of the subjects who satisfied the study criteria were scanned using the Cirrus HD-OCT system with software version 5.0.

Retinal nerve fiber layer thickness measurements were obtained from software supplied by the manufacturer.

Measures of neuroretinal rim thickness (NRT), disc area, average cup-to-disc (C/D) ratio, and cup volume were obtained from the scans.

Statistical analysis

At the end of the study, data were statistically described using analysis of variance (ANOVA) tests by SPSS (Statistical Package for Social Science) program version 20.

Person correlation was used to measure correlation between different continuous variables. P value <0.05 was considered statistically significant.

Results

Age distribution is given in table1 as the following; the mean age was 35.3 ± 3.24 years, with the minimum age 30.00 years and the maximum age 40.00 years.

Table 1: Age distribution

	N	Minimum	Maximum	Mean	SD
Age	30	30.00	40.00	35.30	3.24

N; Number, SD; standard deviation.

In this study, the mean spherical equivalent (SE) value was -8.54 ± 5.39D; with the maximum value of SE -17.88D and the minimum value -3.00D as in (Table 2). The average axial length was 25.99± 2.03 mm; with the maximum axial length value 30.16 mm and the minimum axial length value 23.00 mm as in (Table 2). The average intraocular pressure was 14.23±1.96 mmHg; with the maximum IOP value 18 mmHg and the minimum value was 10 mmHg as shown in Table 2.

Table 2: Spherical equivalent, intraocular pressure and axial length.

	Minimum	Maximum	Mean	SD
SE	-3.00	-17.88	-8.54	5.39
IOP	10.00	18.00	14.23	1.96
AL	23.00	30.16	25.99	2.03

SE; Spherical equivalent, IOP; Intraocular pressure, AL; Axial length, SD; Standard deviation.

In this study there was statistically significant difference between males and females in SE; with the mean value of -4.2 ± 1.5 D in males and -9.7 ± 5.4 D in females (P= 0.00) as in (table 3). There was also statistically significant difference in IOP between males and females; with the mean value of 14.5 ±1.0 mmHg in males and 14.2 ± 2.1 mmHg in females (P= 0.047) as in (Table 3). Also, there was statistically significant difference in AL between males and females; with the mean value of 24.3 ± 1.4 mm in males and 26.1 ± 2.0 mm in females (P= 0.047) as shown in Table 3.

Table (3): Relation between gender and spherical equivalent, intraocular pressure and axial length.

	Gender		Independent t test	P
	Male	Female		
	Mean ± SD	Mean ± SD		
SE	**-4.2 ± 1.5**	**-9.7 ± 5.4**	**4.398**	**.000***
IOP	**14.5 ±1.0**	**14.2 ± 2.1**	**-2.078**	**.047***
AL	**24.3 ± 1.4**	**26.1 ± 2.0**	**-2.078**	**.047***

SE; Spherical equivalent, IOP; intra ocular pressure, AL; axial length, SD; standard deviation, P; p- value < 0.05 is considered statistically significant, t test; Independent t test.

The average RNFL thickness was 88.40±10.61microns; with the maximum average RNFL thickness value, 107.00 microns and the minimum value 64.00 microns as in (table 4). The mean inferior RNFLT was 110.17±22.65 microns; with maximum value, 164.00 microns and the minimum value 74.00 microns as in (Table 4). The mean superior RNFLT was 108.27±15.39 microns; with the maximum value, 134.00 microns and the minimum value 80.00 microns. The mean nasal RNFLT was 71.40±17.77 microns; with the maximum value, 121.00microns and the minimum value 47.00 microns as in (Table 4). The mean temporal RNFLT was 67.53±12.73 microns; with the maximum value 99.00 microns and the minimum value 37.00 microns as shown in Table 4.

Table 4: Retinal nerve fiber layer thickness.

	Minimum	Maximum	Mean	SD
average RNFLT	64.00	107.00	88.40	10.61
Inf. RNFLT	74.00	164.00	110.17	22.65
Sup. RNFLT	80.00	134.00	108.27	15.39
Nasal RNFLT	47.00	121.00	71.40	17.77
Temporal RNFLT	37.00	99.00	67.53	12.73

RNFLT; Retinal nerve fiber layer thickness, Inf.; Inferior, Sup.; Superior, SD; Standard deviation.

Correlation between axial length and RNFL thickness

This study found that there was a weak negative correlation between average RNFLT and AL (r = -0.39, p = 0.04) as in (Table 5).

In this study there was also a statistically significant negative correlation between the superior RNFLT and AL (r = -0.37, p = 0.05) as in (table5).

In this study there was statistically non-significant correlation between nasal RNFLT and AL (r = 0.06, p = 0.74) as in (Table 5); and between temporal RNFLT and AL (r = -0.17, p=0.36) as shown in Table 5.

Table 5: Correlation between axial length and retinal nerve fiber layer thickness.

	AL	
	r*	**P value**
average RNFLT	-0.39	0.04 S
Inf. RNFLT	-0.50	0.01 HS
Sup. RNFLT	-0.37	0.05 S
Nasal RNFLT	0.06	0.74 NS
Temporal RNFLT	-0.17	0.36 NS

AL; Axial length, r; Person correlation coefficient, RNFLT; Retinal nerve fiber layer thickness, P value; p- value < 0.05 is considered statistically significant, Inf.; Inferior, Sup.; Superior.*

Optic disc size measurements result

In this study, the mean disc area was 1.80±0.29mm^2; with the maximum disc area value 2.40 mm^2 and the minimum value 1.39 mm^2 as in (table 6). The average rim area was 1.41±0.33mm^2; with the maximum rim area value 2.20 mm^2 and the minimum value 0.84 mm 2 as in (Table 6). The average cup/disc ratios (CDRs) were 0.42±0.27; with the maximum CDR value 0.95 and the minimum value 0.06 as shown in table 6.

Table 6: Optic disc size measurements.

	Minimum	Maximum	Mean	SD
Disc area	1.39	2.40	1.80	0.29
Rim area	0.84	2.20	1.41	0.33
C/D ratio	0.06	0.95	0.42	0.27

SD; Standard deviation, C/D ratio; Cup-disc ratio.

Correlation between AL and optic disc size measurements

This study found that there was a weak positive correlation between optic disc area and axial length (r = 0.35, p = 0.036) as in (Table 7).

In this study there was statistically non-significant correlation between rim area and axial length (r = -0.09, p=0.65); and between average cup-disc ratio and axial length (r = -0.01, p=0.97) as shown in Table 7.

Table 7: Correlation between axial length and optic disc size measurements.

	AL	
	r*	**P value**
Disc area	0.35	0.036
Rim area	0.09	0.65 NS
C/D ratio	-0.01	0.97 NS

r; Pearson correlation coefficient, AL; Axial length, C/D ratio; Cup disc ratio, P value; p- value < 0.05 is considered statistically significant.*

Linear regression for assessing the relation between AL and other measurements

In this study there was a statistically significant linear regression relationship between AL and (average & inferior) RNFL thickness, disc area (Table 8); Where:

- The coefficient (B) indicates that for every additional unit in AL you can expect average RNFLT to decrease by an average of 1.961 units.
- The coefficient (B) indicates that for every additional unit in AL you can expect inf. RNFLT to decrease by an average of 5.815 units.
- The coefficient (B) indicates that for every additional unit in AL you can expect disc area to increase by an average of.056 units.

Table (8): Linear regression for assessing the relation between AL and other measurements.

	R Square (r^2)	B	P
AL and average RNFLT	0.136	-1.961	0.045*
Inf. RNFLT	0.262	-5.815	0.004*
Sup. RNFLT	0.114	-2.602	0.068
Nasal RNFLT	0.006	0.683	0.687
Temporal RNFLT	0.028	-1.060	0.381
disc area	0.148	0.056	0.036*
rim area	0.007	0.014	0.657
c\d ratio	0.000	0.002	0.925

P; p-value is significant ≤ 0.05, (*); statistically significant, B; Regression coefficient.

4. Discussion

The increasing prevalence of myopia has been raising concern over its impact on public health since it is associated with various sight - threatening ocular conditions[8].

Examining the retinal nerve fiber layer (RNFL) is highly valuable in the diagnosis of optic nerve anomalies and diseases, since the retinal ganglion cell axons continue into the optic nerve fibers behind the optic nerve head[9].

This cross-sectional study assessed the effect of axial length (AL) in myopic patients on RNFL thickness and ONH measurements.

Thirty eyes of 15 myopic patients were included in this study. The participants were predominantly females, with a mean age of 35.3 years.

This goes with ***Linke et al. in 2013***[10] in which the mean age was 35.9 years (ranging from 18 to 74 years).

In the current study, the mean SE of the enrolled patients was -8.54 ± 5.39 D reflecting a high myopia. This study also found a statistically significant difference in SE between males and females, as females had a significantly higher SE compared to males.

Similarly, ***Linke et al in 2013***[10] reported that myopic females had a higher SE than males. This can be attributed to the higher prevalence and higher progression of myopia in female patients compared to their male counterparts.

In fact, ***Saw et al in 2008***[11]; ***Lu et al in 2009***[12] and ***Shih et al.***[13] repeatedly reported that when females develop myopia, they tend to have a more severe condition compared to males.

However, the same finding was not found among other age groups. Moreover, the ***COMET study in 2013***[14] showed that men have a slower progression rate of myopia compared to women, which supports the finding of an increased female prevalence of myopia at age 20–39.

Regarding the axial length (AL), patients in this study had a mean axial length of 25.99 ±2.04 mm.

Similarly, ***Ahmed el al., 2017***[15] cross sectional study with the mean AL of 25.73 ± 1.14 mm.

Moreover, this study found that AL was significantly associated with the gender of the patient, as myopic females had a significantly longer AL compared to males.

Although ***Olsen et al in 2007***[16]***; Warrier et al in 2008***[17] agreedin the literature that women tend to have a shorter AL, partly explained by their shorter stature.

However, ***Ohsugi et al in 2017***[18] reported that in myopic patients, female patients showed a greater increase in their AL per year compared to their male counterparts, which explains this study finding.

In this study, the average intraocular pressure (IOP) was 14.23±1.96 mmHg. Moreover, this study found a statistically significant difference in IOP between males and females, as males had a higher IOP compared to females.

The reports of such an association in the literature have been conflicting. For instance, this study finding is consistent with ***Hoehn et al., 2013***[19] and ***Cohen et al., 2016***[20] studies, who reported significantly higher IOP values in males.

However, and contrary to this study findings, ***Pointer in 2000***[21]; ***Abraham and Thomas in***

2015[22] and ***Louisraj et al in 2018***[23]***;*** *have found IOP to be* higher in females.

Qureshi in 1997[24] and ***Patel et al in 2018]25[;*** attributed this difference to the effect of hormones, since estrogen may have an effect on the inflow of aqueous humor, the ciliary body, and the trabecular meshwork.

In general, this study found that the average RNFL thickness had a weak negative correlation with axial length, as The RNFL thickness decreased with increasing axial length; the average RNFLT decrease with increase the AL and the degree of myopia.

Several studies documented the average RNFL thickness in normal eyes and eyes with different degrees of myopia and found that RNFL thickness decreased with increasing severity of myopia. For example, in an early study*,* ***Leung et al in 2006***[26] found that RNFL thickness was lower in highly myopic eyes than in eyes with low to moderate myopia.

Based on their findings, ***Zha et al in 2017***[27] proposed that the average RNFL thickness has a linear increase with the increase of SE.

As a matter of fact, ***Zhao et al., 2014***[28] reported that RNFLT decreased by 1 μm (1%) per dioptre of myopia. This observation, along with the difference in samples and population's age, can explain the thinner average RNFL in this study (88.4 μm, SE −8.54 D), when compared with ***Zha et al., 2017***[27] (100.08 μm, SE −2.96 D).

In this study the mean inferior, superior, nasal and temporal RNFL thicknesses were 110.17±22.65, 108.27±15.39, 71.40 ±17.77 and 67.53±12.73 mm respectively. The thickest was the inferior RNFL followed by the superior RNFL then the nasal RNFL and the thinnest was the temporal RNFL.

This is consistent with ***Alasil et al in 2013***[29] found that the inferior quadrant had the thickest RNFL measurements (126± 15.8), followed by the superior (117.2± 16.3), nasal, (75± 14) and temporal (70.6± 10.8) quadrants.

However, ***Zhao et al in 2014***[28] and ***Zha et al in 2017***[27] reported that RNFL thickness was the highest at the temporal quadrant and the lowest at the nasal quadrant.

This study found statistically significant negative correlation between the superior and the inferior RNFLT and the AL; while there was statistically insignificant correlation between the nasal and temporal RNFLT and the AL.

Similar to this study results, ***Rauscher et al in 2009***[30] found that RNFL thickness decreased with higher axial length. They also indicated that the average, superior and inferior RNFL thickness significantly decreased with higher axial length and higher SE.

Meanwhile, ***Garcia-Valenzuela et al., 2002***[31]***; Hoh et al., 2006***[32] and ***Melo et al., 2006***[3] studies did not find significant associations between AL and RNFL thickness. This can be explained by the earlier generation time-domain OCT used in these studies, which may have limited the resolution and lowered sensitivity.

This study found the same correlation insignificant at the nasal or temporal quadrant.

Similarly, ***Peng et al in 2017***[33] and ***Chen et al., 2018***[34]reported insignificant correlations between AL and RNFL of the temporal and nasal quadrants.

On the other hand, ***Wang et al in 2011***[35] and ***Knight et al in 2012***[36] reported a significant positive correlation between AL and RFNL within the temporal or the nasal quadrants.

The mean optic disc area in the current study was 1.80±0.29. This study found a positive correlation between optic disc area and axial length; the optic disc area increased with increase the AL.

Similarly, ***Oliveira et al in 2007***[37] and ***Leung et al in 2007***[38] found that optic disc area increased with AL in normal eyes and myopic eyes as well.

Meanwhile, ***Tomais et al in 2008***[39] reported that such correlation between axial length and optic disc area was insignificant. However, this can be attributed to the different age group and the equal gender distribution in their study compared to this study, which might explain this inconsistency in results.

Concerning the other ONH parameters, this study found that the average rim area was 1.41±0.33 mm^2.

As for the correlations, both parameters were not significantly correlated with AL. This is similar to ***Lima et al., 2011***[40] study, which indicated that the correlation between AL and rim area was insignificant.

However, ***Savini et al in 2011***[41] and ***Bae et al in 2016***[42] have found rim area and CDR to be negatively correlated with AL.

This study has some limitations. First, the number of enrolled subjects was small, which may have hindered the power of the study. Second, it was conducted in a single hospital, and therefore, our findings don't represent the Egyptian population and cannot be generalized. Third, due to the limited time frame, we used a cross-section study design. Such design has its weaknesses; especially the difficulty of interpreting the reported associations.

In conclusion, this study found that AL had a negative correlation with average RNFLT and that of superior and inferior quadrants, and a positive correlation with optic disc area. However, AL was not significantly correlated with RNFL thickness in the nasal or temporal quadrant, optic rim area, or CDR.

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